

Applicant	:	Paul G. Yock, et al.
Appl. No.	:	Not yet assigned. Reissue of US Patent No. 6,346,098 B1
Examiner	:	Not yet assigned.
Docket No.	:	13854.4004

### Remarks

This preliminary amendment concerns the reissue application submitted herewith. By this amendment, original claims 8, 11, 15, and 19 are amended, and new claims 20 through 100 are added.

The claim amendments are minor. The amendment to claim 8 changes the word "vessel" to "vein", in order to reconcile the recitation with its antecedent. The amendment to claim 11 corrects the misspelling of "inflammation," and also changes "vessel" to "vein" to reconcile with the recitation in the independent claim. The amendment to claim 15 changes the word "on" in the phrase "on said vein" to, more appropriately, "in". Finally, the amendment to claim 19, like the amendment to claim 11, corrects the misspelling of "inflammation" and changes "vessel" to "vein" to reconcile with the recitation in the independent claim.

The new claims, 20 through 100, are intended to correct the errors discussed in the Joint Declaration of the Inventors submitted herewith. Of these claims, claims 20 through 36 all depend (either directly or indirectly) from original claim 1. Claims 37 through 55 generally track original claims 1 through 19, but include recitation of retroinfusing "a fluid" rather than retroinfusing "said agent," thereby broadening those claims relative to the original patent claims. New independent claim 56 generally tracks original claim 7, but clarifies that the mechanical stress "facilitates the transport of said agent through the wall of said vessel." New independent claim 67 generally tracks original claim 13, but similarly clarifies that the distention "facilitates the transport of said agent through the wall of said

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vessel." New independent claim 78 generally tracks original claim 7, but (like new independent claim 56) clarifies that the mechanical stress "facilitates the transport of said agent through the wall of said vessel." New claim 78 (and its dependent claims, 79-89) also includes recitation of retroinfusing "a fluid" rather than retroinfusing "said agent", thereby broadening those claims relative to the original claims. Finally, new independent claim 90 generally tracks original claim 13, but (like new independent claim 67) clarifies that the mechanical stress "facilitates the transport of said agent through the wall of said vessel." New claim 90 (and its dependent claims, 91-100) also includes recitation of retroinfusing "a fluid" rather than retroinfusing "said agent", thereby broadening those claims relative to the original claims.

Specification support for all of the amendments and new claims is listed in the Statement of Status / Support for Changes to Claims submitted herewith. No new matter is added by this amendment.

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### CONCLUSION

In view of the foregoing, it is submitted that the claims presented in this reissue application define patentable subject matter to which Applicant is entitled. Accordingly, consideration and allowance of the reissue application is requested.

Respectfully submitted,

Orrick, Herrington & Sutcliffe LLP

Dated: Feb. 3, 2004

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : Not yet assigned. Confirmation No.:  
Reissue of US Patent No.  
6,346,098 B1  
Applicant : Paul G. Yock, et al.  
Filing Date : Herewith  
Title : METHODS AND KITS FOR LOCALLY ADMINISTERING AN  
ACTIVE AGENT TO AN INTERSTITIAL SPACE OF A HOST  
Group Art Unit : Not yet assigned.  
Examiner : Not yet assigned  
Docket No. : 13854.4004  
Customer No. : 34313

Commissioner for Patents  
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P.O. Box 1450  
Alexandria, VA 22313-1450

**STATEMENT OF STATUS / SUPPORT FOR CHANGES TO CLAIMS**  
**UNDER 37 C.F.R. § 1.173(c)**

Dear Sir/Madam:

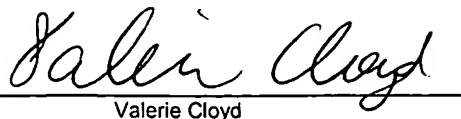
In connection with the Application for Reissue and Preliminary Amendment filed herewith, the following is a statement of status of all patent claims and of all added claims as of the date of the Preliminary Amendment, and an explanation of the support in the disclosure of the patent for the changes made to the claims.

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CERTIFICATE OF MAILING  
37 CFR §1.10

Date: February 9, 2004  
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I hereby certify that on the dated listed above, this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service in accordance with 37 C.F.R. § 1.10 as "Express Mail Post Office to Addressee," with sufficient postage in an envelope addressed to: Mail Stop Patent Application, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

  
Valerie Cloyd

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### **Status of Claims**

As of the date of the Preliminary Amendment submitted herewith, the status of the claims is as follows:

Claims 1 through 100 are pending.

### **Support for Changes Made to Claims**

Of the pending claims, the following changes have been made by the Preliminary Amendment submitted herewith:

Claims 8, 11, 15, and 19 have been amended.

Claims 20 through 100 have been added.

The support in the disclosure of the patent for each of the above changes is set forth in the table below.

<b><u>Amended / New Claim</u></b>	<b><u>Support in Patent Disclosure</u></b>
8. (Amended) A method of locally administering an active agent to a host, said method comprising: retroinfusing said agent into a vein of said host under conditions sufficient to produce a disruption in said [vessel] <u>vein</u> and for said agent to enter an interstitial space of said host through said disruption so that said agent is locally administered to said host.	Amendment is to correct error in claim because there is no antecedent for "said vessel" in claim. The proper antecedent is "vein" rather than "vessel." Support for "vein" appears at col. 3, line 18, and col. 2, line 22.
11. (Amended) The method according to claim 8, wherein said method further comprises producing [inflammation] <u>inflammation</u> in said [vascular vessel] <u>vein</u> .	Same as Claim 8, plus correction of spelling of "inflammation." Col. 4, lines 62-64.

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<b><u>Amended / New Claim</u></b>	<b><u>Support in Patent Disclosure</u></b>
<p>15. (Amended) A method of locally administering an active agent to a host, said method comprising:  retroinfusing said agent into a vein of said host with a catheter and at a pressure sufficient to produce a disruption [on] <u>in</u> said vein such that said agent enters an interstitial space proximal to the vein through said disruption;  whereby said agent is locally administered to said host.</p>	Amendment corrects grammatical error.
<p>19. (Amended) The method according to claim 16, wherein said method further comprises producing [inflammation] <u>inflammation</u> in said [vascular vessel] <u>vein</u>.</p>	Same as Claim 11.
<p>20. The method of claim 1 wherein said agent comprises cells.</p>	Col. 8, line 37.
<p>21. The method of claim 1 wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.</p>	Col. 7, lines 52 and 53.
<p>22. The method of claim 1 wherein said agent comprises therapeutic nucleic acids.</p>	Col. 7, line 55.
<p>23. The method of claim 22 wherein the therapeutic nucleic acids comprise at least one gene.</p>	Col. 7, line 58.
<p>24. The method of claim 1 wherein said agent comprises a dye or an imaging agent.</p>	Col. 8, lines 28-31.

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<b><u>Amended / New Claim</u></b>	<b><u>Support in Patent Disclosure</u></b>
25. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 50 mm Hg.	Col. 5, line 56.
26. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 60 mm Hg.	Col. 5, line 56.
27. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 1000 mm Hg.	Col. 5, line 58.
28. The method of claim 5 wherein the energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.	Col. 6, lines 13-47.
29. The method of claim 3 wherein said stress is chemical stress.	Col. 6, lines 48-51.
30. The method of claim 1 wherein said vessel is an artery.	Col. 3, line 18.
31. The method of claim 2 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
32. The method of claim 1 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.

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<b>Amended / New Claim</b>	<b>Support in Patent Disclosure</b>
33. The method of claim 32 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-12.
34. The method of claim 2 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
35. The method of claim 35 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.
36. The method of claim 1 wherein said pressure is sufficient to at least distend said vessel.	Col. 5, lines 19-23.
37. A method of locally administering an active agent to a host, said method comprising: retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to produce a disruption in said vessel and infusing said agent into an interstitial space of said host through said disruption and locally administering said agent to said host through said disruption.	Col. 4, line 54.
38. The method according to claim 37, wherein said vessel is a vein.	Col. 2, line 22.



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<b><u>Amended / New Claim</u></b>	<b><u>Support in Patent Disclosure</u></b>
39. The method according to claim 37, wherein said retroinfusing comprises providing stress to said vascular vessel at a site proximal to said interstitial space.	Col. 2, lines 21-24
40. The method according to claim 37, wherein said method further comprises using depot means.	Col. 9, lines 1 and 2.
41. The method according to claim 37, wherein said method further comprises administration of energy to said vessel.	Col. 6, lines 1-8.
42. The method according to claim 37, wherein said interstitial space is myocardial interstitial space.	Col. 4, line 34.
43. The method according to claim 39, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.	Col. 1, line 66 – Col. 2, line 2.
44. A method of locally administering an active agent to a host, said method comprising: retroinfusing a fluid into a vein of said host under conditions sufficient to produce a disruption in said vein and infusing said agent into an interstitial space of said host through said disruption so that said agent is locally administered to said host.	Col. 4, lines 52-55.

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<b>Amended / New Claim</b>	<b>Support in Patent Disclosure</b>
45. The method according to claim 44, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vein.	Col. 1, line 66 – Col. 2, line 2.
46. The method according to claim 44, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
47. The method according to claim 44, wherein said method further comprises producing inflammation in said vein.	Col. 4, lines 62-64.
48. The method according to claim 44, wherein said interstitial space is myocardial interstitial space.	Col. 4, line 34.
49. The method according to claim 45, wherein said pressure is sufficient to at least distend said vein.	Col. 5, lines 19-23.
50. The method according to claim 45, wherein said pressure is sufficient to disrupt said vein.	Col. 5, lines 35-36.

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Amended / New Claim	Support in Patent Disclosure
<p>51. A method of locally administering an active agent to a host, said method comprising:  retroinfusing a fluid into a vein of said host with a catheter and at a pressure sufficient to produce a disruption in said vein and infusing said agent into an interstitial space proximal to the vein through said disruption;  whereby said agent is locally administered to said host.</p>	<p>Col. 4, line 54.</p>
<p>52. The method according to claim 51, wherein said pressure is sufficient to at least distend said vein.</p>	<p>Col. 5, lines 19-23.</p>
<p>53. The method according to claim 52, wherein said pressure is sufficient to disrupt said vein.</p>	<p>Col. 5, lines 35-36.</p>
<p>54. The method according to claim 52, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.</p>	<p>Col. 7, lines 52 and 53.</p>
<p>55. The method according to claim 52, wherein said method further comprises producing inflammation in said vein.</p>	<p>Col. 4, lines 62-64.</p>

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<b><u>Amended / New Claim</u></b>	<b><u>Support in Patent Disclosure</u></b>
56. A method of locally administering an active agent to a host, said method comprising: retroinfusing said agent into a vascular vessel of said host under conditions sufficient to produce at least a mechanical stress on said vessel, which stress facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.	Col. 4, line 54.
57. The method according to claim 56, wherein said pressure is sufficient to at least distend said vessel.	Col. 5, lines 19-23.
58. The method according to claim 56, wherein said pressure is sufficient to disrupt said vessel.	Col. 5, lines 35-36.
59. The method according to claim 56, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
60. The method according to claim 56, wherein said method further comprises producing inflammation in said vessel.	Col. 4, lines 62-64.
61. The method of claim 56 wherein said vessel is an artery.	Col. 3, line 18.

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<b>Amended / New Claim</b>	<b>Support in Patent Disclosure</b>
62. The method of claim 58 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
63. The method of claim 56 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
64. The method of claim 63 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-12.
65. The method of claim 58 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
66. The method of claim 65 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

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<b><u>Amended / New Claim</u></b>	<b><u>Support in Patent Disclosure</u></b>
67. A method of locally administering an active agent to a host, said method comprising: retroinfusing said agent into a vascular vessel of said host under conditions sufficient to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.	Col. 5, lines 19-23.
68. The method according to claim 67, wherein said retrofusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.	Col. 1, line 66 – Col. 2, line 2.
69. The method according to claim 67, wherein said pressure is sufficient to disrupt said vessel.	Col. 5, lines 35-36.
70. The method according to claim 67, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
71. The method according to claim 67, wherein said method further comprises producing inflammation in said vessel.	Col. 4, lines 62-64.
72. The method of claim 67 wherein said vessel is an artery.	Col. 3, line 18.

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<b><u>Amended / New Claim</u></b>	<b><u>Support in Patent Disclosure</u></b>
73. The method of claim 69 wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
74. The method of claim 67 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
75. The method of claim 74 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-13.
76. The method of claim 69, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
77. The method of claim 76, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

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<b>Amended / New Claim</b>	<b>Support in Patent Disclosure</b>
<p>78. A method of locally administering an active agent to a host, said method comprising:</p> <p>retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to produce a mechanical stress in said vessel, which stress facilitates the transport of said agent through a wall of said vessel so that said agent is locally administered to said host.</p>	<p>Col. 4, line 54; Col. 1, line 66 – Col. 2, line 2.</p>
<p>79. The method according to claim 78, wherein said vessel is a vein.</p>	<p>Col. 2, line 22.</p>
<p>80. The method according to claim 78, wherein said pressure is sufficient to at least distend said vessel.</p>	<p>Col. 5, lines 19-23.</p>
<p>81. The method according to claim 78, wherein said pressure is sufficient to disrupt said vessel.</p>	<p>Col. 5, lines 35-36.</p>
<p>82. The method according to claim 78, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.</p>	<p>Col. 7, lines 52 and 53.</p>
<p>83. The method according to claim 78, wherein said method further comprises producing inflammation in said vessel.</p>	<p>Col. 4, lines 62-64.</p>
<p>84. The method of claim 78 wherein said vessel is an artery.</p>	<p>Col. 3, line 18.</p>



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<b><u>Amended / New Claim</u></b>	<b><u>Support in Patent Disclosure</u></b>
85. The method of claim 78 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
86. The method of claim 78 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
87. The method of claim 86 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-12.
88. The method of claim 81 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
89. The method of claim 88 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

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<b><u>Amended / New Claim</u></b>	<b><u>Support in Patent Disclosure</u></b>
<p>90. A method of locally administering an active agent to a host, said method comprising:</p> <p>retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.</p>	Col. 5, lines 19-23; Col. 1, line 66 – Col. 2, line 2.
<p>91. The method according to claim 90, wherein said vessel is a vein.</p>	Col. 2, line 22.
<p>92. The method according to claim 90, wherein said pressure is sufficient to disrupt said vessel.</p>	Col. 5, lines 35-36.
<p>93. The method according to claim 90, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.</p>	Col. 7, lines 52 and 53.
<p>94. The method according to claim 90, wherein said method further comprises producing inflammation in said vessel.</p>	Col. 4, lines 62-64.
<p>95. The method of claim 90 wherein said vessel is an artery.</p>	Col. 3, line 18.

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<u>Amended / New Claim</u>	<u>Support in Patent Disclosure</u>
96. The method of claim 92 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
97. The method of claim 90 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
98. The method of claim 97 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-13.
99. The method of claim 92, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.

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<u>Amended / New Claim</u>	<u>Support in Patent Disclosure</u>
100. The method of claim 99, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

Respectfully submitted,

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